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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/708,506	11/09/2000	Arno Hartmann	MERCK-2056	2626

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EXAMINER

DEBERRY, REGINA M

ART UNIT PAPER NUMBER

1647

DATE MAILED: 01/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/708,506

Applicant(s)

HARTMANN ET AL.

Examiner

Regina M. DeBerry

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 01 November 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 2-4, 16-18, 24, 25, 27, 30, 32, 33 and 35-41 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-4, 16-18, 24, 25, 27, 30, 32, 33 and 35-41 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

***Status of Application, Amendments and/or Claims***

The amendment filed 01 November 2005 has been entered in full. Claims 1, 5-15, 19-23, 26, 28, 29, 31 and 34 are cancelled. New claim 41 was added.

Claims 2-4, 16-18, 24, 25, 27, 30, 32, 33, 35-41 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Withdrawn Objections And/Or Rejections***

The rejection to claims 2-4, 16-18, 24, 25, 27-30, 32, 33, 35 and 39 under 35 U.S.C. 103(a) as being unpatentable over Sytkowski *et al.* WO 99/02709 in view of Cox, III, U.S. Patent 6,608,183 B1, as set forth at pages 3-5 of the previous Office Action (02 June 2005), is *withdrawn* in view of the amendment (01 November 2005).

The rejection to claim 29 under 35 U.S.C. 103(a) as being unpatentable over Sytkowski *et al.* WO 99/02709 in view of Cox, III, U.S. Patent 6,608,183 B1 as applied to claims 28, 30, 32, 33, above, and further in view of Okasinski *et al.*, U.S. Patent 5,888,772, as set forth at pages 5-6 of the previous Office Action (02 June 2005), is *withdrawn* in view of the amendment (01 November 2005).

The rejection to claims 36-38 under 35 U.S.C. 103(a) as being unpatentable over Sytkowski *et al.* WO 99/02709 in view of Cox, III, U.S. Patent 6,608,183 B1 as applied to claim 30 above, and further in view of Bolt *et al.*, U.S. 5,585,097, as set forth at pages 6-7 of the previous Office Action (02 June 2005), is *withdrawn* in view of the amendment (01 November 2005).

The objection to claims 27 and 40, as set forth at page 7 of the previous Office Action (02 June 2005), is *withdrawn* in view of the amendment (01 November 2005).

**Matter of Record**

Please note that the 35 U.S.C. 103 rejections cited above were withdrawn because of the new limitations in the amended claim. These rejections will be reapplied to the claims if the claim language is amended. Please see the 35 U.S.C. 112, first paragraph, written description, new matter rejection below.

**NEW REJECTIONS:**

**Claim Rejections - 35 USC § 112, First Paragraph, Written Description, New Matter**

Claims 2-4, 16-18, 24, 25, 27, 30, 32, 33, 35-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

The specification as originally filed does not provide support for the invention as now claimed: "...so that the substituted Cys may form a disulfide bond with a Cys corresponding to position 29 of human erythropoietin.." (claim 30).

Applicant's amendment, filed 01 November 2005, asserts that no new matter has been added and directs support to page 13, lines 13-21 for the written description for

the above-mentioned "limitations". However, the exact wording or connotation of the instant claim is not readily apparent from said sections.

The specification as filed does not provide a written description or set forth the metes and bounds of this "limitations". The instant claims now recite limitations which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as-filed. Applicant is required to cancel the new matter in the response to this Office action. Alternatively, Applicant is invited to provide specific written support for the "limitations" indicated above or rely upon the limitations set forth in the specification as filed.

#### **Claim Rejections - 35 USC § 112, First Paragraph, Enablement**

Claims 2-4, 16-18, 24, 25, 27, 30, 32, 33, 35-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 30 recites, "...an amino acid other than Cys at a position corresponding to position 33 of human erythropoietin..". While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship. The art fails to teach that position 33 of human

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erythropoietin can be substituted with **any** amino acid. For instance, Boissel *et al.* (JBC Vol. 268/1993, reference of record) teach that when cysteine at position 33 was change to a proline (as recited in instant claim 41) by site directed mutagenesis in human erythropoietin, the protein had **greatly reduced** *in vitro* biological activity (page 15990, 1st-6th lines). The instant claims recite the limitation, "retains erythropoietin activity". The instant claims are not enabled for these limitations because the art of record teaches otherwise.

Due to the large quantity of experimentation necessary to generate the derivatives recited in the claim and screen same for erythropoietin activity, the lack of direction/guidance presented in the specification regarding how to use EPOs that do not retain erythropoietin activity, the absence of working examples directed to same, the complex nature of the invention and the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

#### **Claim Rejections - 35 USC § 112, Second Paragraph**

Claims 2-4 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claim 30 is indefinite because of the recitation, "...the EPO portion comprises a substituted Cys at position corresponding to Gln86, Pro87, Trp88, Gln89 or Leu91 of

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human erythropoietin and an amino acid other than Cys at a position corresponding to position 33 of human erythropoietin so that the substituted Cys may form a disulfide bond with a Cys corresponding to position 29 of human erythropoietin". The instant claim is indefinite because it is not clear *which* substituted Cys position (Gln86, Pro87, Trp88, Gln89 or Leu91) may form a disulfide bond with Cys at position 29.

Claims 2-4 are indefinite because they depend from a cancelled claim (claim 28).

### ***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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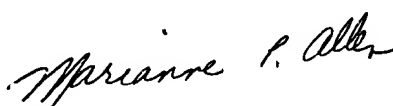
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



RMD  
1/18/06

  
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1/19/06  
AU1647